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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/616,284	07/14/00	GOLD L	NEX77/CIP2

EXAMINER	
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1655	8

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HM12/0815

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/616,284	GOLD ET AL.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to Comply w/ Segun Rules

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-17, drawn to a method for automated identification of a nucleic acid ligand, classified in class 435, subclass 6.

   II. Claim 17, drawn to an apparatus for automated identification of a nucleic acid ligand, classified in class 422, subclass 100.

   III. Claims 18 and 19, drawn to a method for identifying a nucleic acid ligand, classified in class 435, subclass 6.

2. The inventions are distinct, each from the other because:

Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the process as claimed can be practiced by another materially different apparatus such as a thermocycler and pipetter.

Inventions III and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the process as claimed can be practiced by another materially different apparatus such as a thermocycler and pipetter.

Inventions I and III are independent and distinct methods. Inventions are independent and distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not disclosed as capable of

use together and they have different modes of operation i.e. the invention of Group I operates by nucleic acid-protein binding and the invention of Group III operates by nucleic acid-protein photoactivated crosslinking.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Rosemary Kellogg on 3 August 2001 a provisional election was made with traverse to prosecute the invention of Group III, claims 18 and 19. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

6. The instant application claims priority as a CIP to co-pending application 09/356,233 filed 07/16/1999, which is a CIP of 09/232,946 filed 01/19/1999, which is a CIP of 08/792,075 filed 01/31/1997 and a CIP of 09/143,190 filed 08/27/1998, which is a CON of 08/469,609 filed 06/06/1995, which is a CON of 07/714,131 filed 01/10/1991, which is a CIP of 07/536,428 filed 06/11/1990. Instant Claims 18 and 19 are drawn to a method for identifying a nucleic acid ligand that photocrosslinks to a protein from a candidate mixture of nucleic acids wherein each member of said candidate mixture contains a photoreactive group and wherein the method steps are performed at one or more work stations by a cartesian

robotic manipulator controlled by a computer. The instantly claimed photocrosslinking and computer controlled robotic manipulator are limitations which were not disclosed in the '075, '190, '609, '131, or '428 applications. Therefore, the effective filing date for instant Claims 18 and 19 is the filing date of the '946 application i.e. 19 January 1999.

Claim Objections

7. Claim 18 is objected to because of the following informalities: The preamble of Claim 18 contains two inappropriate periods; in line 2 after "nucleic acids" and inline 3 after "group".

Appropriate correction is required.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cox et al (Biotechnology. Prog. 1998, 14:845-850) in view of Hanna (Methods in Enzymology, 1989, 180: 383-405).

Regarding Claim 18, Cox et al. teach a method for identifying a nucleic acid ligand from a candidate mixture wherein the ligand interacts with a target (Abstract lines 1-4 and page 845, left column, second paragraph, lines 1-5) the method comprising: contacting the candidate mixture with the target (page 846-847, "Selection Regime"); partitioning the nucleic

acid-target complexes (page 847, left column, lines 1-19); and identifying the nucleic acid ligand (page 847, right column, first full paragraph) and wherein method steps are performed at one or more work stations on a work surface by a Cartesian robotic manipulator i.e. manipulate liquids in an x-y-z axis (page 847, right column, second full paragraph) controlled by a computer (page 845, right column, last 3 lines and page 846, left column, lines 1-11). Cox et al. do not teach the nucleic acid ligand contains a photoreactive group and irradiating the nucleic acid–target complex to photocrosslink the nucleic acid-protein. However, modifying a nucleic acid with a photoreactive group and irradiating to thereby photocrosslink modified nucleic acid-protein complexes was well known in the art at the time the claimed invention was made as taught by Hanna. Specifically, Hanna teaches a method for identifying a nucleic acid that photocrosslinks to a protein comprising: contacting a candidate mixture of nucleic acids with a protein; irradiating to photocrosslink nucleic acid-protein complexes; partitioning the photocrosslinked nucleic acid-protein complexes (page 405, last paragraph-page 406, fifth full paragraph, Isolation and Analysis); and identifying a nucleic acid photocrosslinked to the protein (page 408, last paragraph-through page 409). Additionally, Hanna teaches that modification of an RNA with photoreactive groups allows for the study of RNA-protein interactions in their native conformations (page 389, third full paragraph, lines 1-3) and that RNA-protein photocrosslinking traps weak or transient RNA-protein interactions which, if not photocrosslinked, might not survive isolation (page 383, lines 7-10). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify nucleic acid-protein complex partitioning taught by Cox et al. by modifying the nucleic acid with photoreative groups and irradiating nucleic acid-protein complexes to photocrosslink the complexes prior to partitioning to thereby obtain nucleic acid-protein complexes in their native conformation and obtain weak or transient nucleic acid-protein interactions as taught by Hanna (page 383, lines 7-10 and page 389, third full paragraph, lines 1-3) for the expected benefit of obtaining otherwise unobtainable complexes.

Regarding Claim 19, Cox et al. teach a method for identifying a nucleic acid ligand from a candidate mixture wherein the ligand interacts with a target as defined by Gold et al. (Abstract lines 1-4 and page 845, left column, second paragraph, lines 1-5) the method comprising: contacting the candidate mixture with the target (page 846-847, "Selection Regime"); partitioning the nucleic acid-target complexes (page 847, left column, lines 1-19); amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids (page 847, left column, second full paragraph) and identifying the nucleic acid ligand (page 847, right column, first full paragraph) and wherein method steps are performed at one or more work stations on a work surface by a Cartesian robotic manipulator i.e. manipulate liquids in an x-y-z axis (page 847, right column, second full paragraph) controlled by a computer (page 845, right column, last 3 lines and page 846, left column, lines 1-11). Cox et al. do not teach the nucleic acid ligand contains a photoreactive group and irradiating the nucleic acid–target complex to photocrosslink the nucleic acid-protein. However, modifying a nucleic acid with a photoreactive group and irradiating to thereby photocrosslink modified nucleic acid-protein complexes was well known in the art at the time the claimed invention was made as taught by Hanna. Specifically, Hanna teaches a method for identifying a nucleic acid that photocrosslinks to a protein comprising: contacting a candidate mixture of nucleic acids with a protein; irradiating to photocrosslink nucleic acid-protein complexes; partitioning the photocrosslinked nucleic acid-protein complexes (page 405, last paragraph-page 406, fifth full paragraph, Isolation and Analysis); and identifying a nucleic acid photocrosslinked to the protein (page 408, last paragraph-through page 409). Additionally, Hanna teaches that modification of an RNA with photoreactive groups allows for the study of RNA-protein interactions in their native conformations (page 389, third full paragraph, lines 1-3) and that RNA-protein photocrosslinking traps weak or transient RNA-protein interactions which, if not photocrosslinked, might not survive isolation (page 383, lines 7-10). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to

modify nucleic acid-protein complex partitioning taught by Cox et al. by modifying the nucleic acid with photoreative groups and irradiating nucleic acid-protein complexes to photocrosslink the complexes prior to partitioning to thereby obtain nucleic acid-protein complexes in their native conformation and obtain weak or transient nucleic acid-protein interactions as taught by Hanna (page 383, lines 7-10 and page 389, third full paragraph, lines 1-3) for the expected benefit of obtaining otherwise unobtainable complexes.

10. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al. (U.S. Patent No. 5,475,096, filed 10 June 1991) in view of Cathcart et al. (U.S. Patent No. 5,443,791, filed 7 August 1992) and Hanna (Methods in Enzymology, 1989, 180: 383-405).

Regarding Claim 18, Gold et al. teach a method for the identification of a nucleic acid ligand from a candidate mixture of nucleic acids (Column 9, lines 14-40, Fig. 2 and Example 1), wherein said nucleic acid ligand binds a protein (Column 13, lines 1-6 and 15-20) the method comprising: contacting the candidate mixture with the protein wherein the nucleic acids having an increased affinity to the protein relative to the candidate mixture to form complexes (Column 36, Example 1, Column 36, lines 58-62); partitioning the increased affinity nucleic acids from the remainder of the candidate mixture (Column 13, lines 21-35 and Example 1, Column 36, lines 58-62); and identifying the nucleic acid ligand (Example 1, Column 37, lines 24-28). Gold et al. do not teach the method is automated wherein method steps are performed at one or more work stations on a work surface by a Cartesian robotic manipulator controlled by a computer. However, automated methods of identifying a nucleic acid from a mixture of nucleic acids were known in the art as taught by Cathcart et al. Specifically, Cathcart et al. teach the method for automated identification of a nucleic acid binding partner from a mixture of nucleic acids using a Cartesian robotic for contacting a nucleic acid binding partner within a mixture of nucleic acids (Fig. 1, #11, Column 13, lines

52-61 and Column 26, lines 20-38); a means for partitioning of nucleic acids having a high affinity for the nucleic acid binding partner using particle-bound affinity pairs (Fig. 1, #26 or 29 and Column 14, lines 9-68); and an identification means for identifying nucleic acid binding partner (Column 26, lines 20-23, Column 27, lines 64-68 and Column 28, lines 1-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply automated machine of Cathcart et al. wherein nucleic acid binding partners are identified to the closely related method of Gold et al. wherein nucleic acid ligands are identified because the skilled practitioner would have known that nucleic acid ligands and nucleic acid binding partners would have the same physical and chemical properties and because one skilled in the art would have known that automated methods produce consistent experimental results, precise manipulations and reduce hands-one operator time as taught by Cathcart et al. (Column 29, lines 50-55) therefore one skilled in the art would have been motivated to apply the automation of Cathcart et al. to the method of Gold et al. for the expected benefits of economy of time and labor. Gold et al. does not teach the nucleic acid ligand contains a photoreactive group and irradiating the nucleic acid–target complex to thereby photocrosslink the nucleic acid-protein complex. However, modifying a nucleic acid with a photoreactive group and irradiating to thereby photocrosslink modified nucleic acid-protein complexes was well known in the art at the time the claimed invention was made as taught by Hanna. Specifically, Hanna teaches a method for identifying a nucleic acid that photocrosslinks to a protein comprising: contacting a candidate mixture of nucleic acids with a protein; irradiating to photocrosslink nucleic acid-protein complexes; partitioning the photocrosslinked nucleic acid-protein complexes (page 405, last paragraph-page 406, fifth full paragraph, Isolation and Analysis); and identifying a nucleic acid photocrosslinked to the protein (page 408, last paragraph-through page 409). Additionally, Hanna teaches that modification of an RNA with photoreactive groups allows for the study of RNA-protein interactions in their native conformations (page 389, third full paragraph, lines 1-3) and that RNA-protein

photocrosslinking traps weak or transient RNA-protein interactions which, if not photocrosslinked, might not survive isolation (page 383, lines 7-10). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify nucleic acid-protein complex partitioning taught by Gold et al. and Cathcart et al. by modifying the nucleic acid with photoreative groups and irradiating nucleic acid-protein complexes to photocrosslink the complexes prior to partitioning to thereby obtain nucleic acid-protein complexes in their native conformation and obtain weak or transient nucleic acid-protein interactions as taught by Hanna (page 383, lines 7-10 and page 389, third full paragraph, lines 1-3) for the expected benefit of obtaining otherwise unobtainable complexes.

Regarding Claim 19, Gold et al. teach a method for the identification of a nucleic acid ligand from a candidate mixture of nucleic acids (Column 9, lines 14-40, Fig. 2 and Example 1), wherein said nucleic acid ligand binds a protein (Column 13, lines 1-6 and 15-20) the method comprising: contacting the candidate mixture with the protein wherein the nucleic acids having an increased affinity to the protein relative to the candidate mixture to form complexes (Column 36, Example 1, Column 36, lines 58-62); partitioning the increased affinity nucleic acids from the remainder of the candidate mixture (Column 13, lines 21-35 and Example 1, Column 36, lines 58-62); amplifying the increased affinity nucleic acids (Column 13, lines 39-47 and Example 1, Column 36, lines 63-68) to yields a ligand-enriched mixture of nucleic acids (Example 1, Column 37, lines 6-22), wherein a nucleic acid ligand is identified (Example 1, Column 37, lines 24-28). Gold et al. do not teach the method is automated wherein method steps are performed at one or more work stations on a work surface by a Cartesian robotic manipulator controlled by a computer. However, automated methods of identifying a nucleic acid from a mixture of nucleic acids were known in the art as taught by Cathcart et al. Specifically, Cathcart et al. teach the method for automated identification of a nucleic acid binding partner from a mixture of nucleic acids using a Cartesian robotic means for contacting a nucleic acid binding partner within a mixture of nucleic acids (Fig. 1, #11,

Column 13, lines 52-61 and Column 26, lines 20-38); a means for partitioning of nucleic acids having a high affinity for the nucleic acid binding partner using particle-bound affinity pairs (Fig. 1, #26 or 29 and Column 14, lines 9-68); and a thermocycling means for amplifying nucleic acids having high affinity for the nucleic acid binding partner (Fig. 1 #21 and Column 7, lines 19-34); and an identification means for identifying nucleic acid binding partner wherein the nucleic acids are labeled (Column 26, lines 20-23, Column 27, lines 64-68 and Column 28, lines 1-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply automated machine of Cathcart et al. wherein nucleic acid binding partners are identified to the closely related method of Gold et al. wherein nucleic acid ligands are identified because the skilled practitioner would have known that nucleic acid ligands and nucleic acid binding partners would have the same physical and chemical properties and because one skilled in the art would have known that automated methods produce consistent experimental results, precise manipulations and reduce hands-one operator time as taught by Cathcart et al. (Column 29, lines 50-55) therefore one skilled in the art would have been motivated to apply the automation of Cathcart et al. to the method of Gold et al. for the expected benefits of economy of time and labor. Gold et al. does not teach the nucleic acid contains a photoreactive group and irradiating the nucleic acid–target complex to thereby photocrosslink the nucleic acid-protein complex. However, modifying a nucleic acid with a photoreactive group and irradiating to thereby photocrosslink modified nucleic acid-protein complexes was well known in the art at the time the claimed invention was made as taught by Hanna. Specifically, Hanna teaches a method for identifying a nucleic acid that photocrosslinks to a protein comprising: contacting a candidate mixture of nucleic acids with a protein; irradiating to photocrosslink nucleic acid-protein complexes; partitioning the photocrosslinked nucleic acid-protein complexes (page 405, last paragraph-page 406, fifth full paragraph, Isolation and Analysis); and identifying a nucleic acid photocrosslinked to the protein (page 408, last paragraph-through page 409). Additionally, Hanna teaches that

modification of an RNA with photoreactive groups allows for the study of RNA-protein interactions in their native conformations (page 389, third full paragraph, lines 1-3) and that RNA-protein photocrosslinking traps weak or transient RNA-protein interactions which, if not photocrosslinked, might not survive isolation (page 383, lines 7-10). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify nucleic acid-protein complex partitioning taught by Gold et al. and Cathcart et al. by modifying the nucleic acid with photoreative groups and irradiating nucleic acid-protein complexes to photocrosslink the complexes prior to partitioning to thereby obtain nucleic acid-protein complexes in their native conformation and obtain weak or transient nucleic acid-protein interactions as taught by Hanna (page 383, lines 7-10 and page 389, third full paragraph, lines 1-3) for the expected benefit of obtaining otherwise unobtainable complexes.

REQUIREMENT TO COMPLY WITH NUCLEIC ACID SEQUENCE RULES

11. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Applicant is given A PERIOD OF TIME CO-EXTENSIVE WITH THE TIME TO REPLY TO THE ABOVE OFFICE ACTION within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition

accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
August 9, 2001

S. Forman
SUPERVISORY PATENT EXAMINER
PRIMARY EXAMINER